

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 08 January 2001 (08.01.01)	
International application No. PCT/GB00/01522	Applicant's or agent's file reference KR/P32293
International filing date (day/month/year) 19 April 2000 (19.04.00)	Priority date (day/month/year) 23 April 1999 (23.04.99)
Applicant BLACKLER, Paul, David, James et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 21 November 2000 (21.11.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Jean-Marc Vivet

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KR/P32293	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 01522	International filing date (day/month/year) 19/04/2000	(Earliest) Priority Date (day/month/year) 23/04/1999
Applicant SMITHKLINE BEECHAM PLC		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

THIAZOLIDINEDIONE DERIVATIVE AND ITS USE AS ANTIDIABETIC

5. With regard to the abstract,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 13, 14 (both partly)

Contrary to the requirements of Article 6 PCT, claims 13 and 14 do not clearly define the matter for which protection is sought. The search with regard to these claims has therefore been limited to the use of a polymorph as defined in claim 1.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01522

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D417/12 A61K31/427 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A ✓	WO 94 05659 A (SMITHKLINE BEECHAM PLC) 17 March 1994 (1994-03-17) cited in the application the whole document, particularly page 2, lines 12-14	1, 10
A ✓	HALEBLIAN J ET AL: "Pharmaceutical application of polymorphism" JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 58, no. 8, 1 August 1969 (1969-08-01), pages 911-929, XP002020518 ISSN: 0022-3549 the whole document	1

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

2 August 2000

Date of mailing of the international search report

16/08/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Allard, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01522

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A ✓	W0 99 31093 A (SMITHKLINE BEECHAM PLC) 24 June 1999 (1999-06-24) cited in the application the whole document ----	1, 10
P, A ✓	W0 99 31094 A (SMITHKLINE BEECHAM PLC) 24 June 1999 (1999-06-24) cited in the application the whole document ----	1, 10
P, A ✓	W0 99 31095 A (SMITHKLINE BEECHAM PLC) 24 June 1999 (1999-06-24) cited in the application the whole document -----	1, 10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/01522

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9405659	A	17-03-1994	AT 182147 T	15-07-1999
			AU 674880 B	16-01-1997
			AU 4973093 A	29-03-1994
			CA 2143849 A	17-03-1994
			CN 1101911 A,B	26-04-1995
			CN 1183275 A	03-06-1998
			CN 1183413 A,B	03-06-1998
			CN 1183276 A	03-06-1998
			CZ 9500565 A	15-11-1995
			DE 69325658 D	19-08-1999
			DE 69325658 T	30-12-1999
			EP 0658161 A	21-06-1995
			EP 0960883 A	01-12-1999
			ES 2133410 T	16-09-1999
			FI 951004 A	03-03-1995
			FI 982413 A	06-11-1998
			GR 3030794 T	30-11-1999
			HU 72639 A	28-05-1996
			IL 106904 A	30-09-1997
			JP 11147885 A	02-06-1999
			JP 2828777 B	25-11-1998
			JP 8501095 T	06-02-1996
			MX 9305397 A	31-01-1995
			NO 950852 A	03-03-1995
			NO 974646 A	03-03-1995
			NZ 255505 A	22-08-1997
			PL 307812 A	26-06-1995
			RU 2128179 C	27-03-1999
			SG 48302 A	17-04-1998
			SI 9300452 A	30-06-1994
			SK 27795 A	09-08-1995
			US 5741803 A	21-04-1998
			US 5910592 A	08-06-1999
			ZA 9306509 A	16-06-1994
WO 9931093	A	24-06-1999	AU 2272299 A	05-07-1999
WO 9931094	A	24-06-1999	AU 2272399 A	05-07-1999
WO 9931095	A	24-06-1999	AU 1967999 A	05-07-1999

PATENT COOPERATION TREATY

PCT

REC'D 22 JUN 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference KR/P32293	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/01522	International filing date (day/month/year) 19/04/2000	Priority date (day/month/year) 23/04/1999
International Patent Classification (IPC) or national classification and IPC C07D417/00		
Applicant SMITHKLINE BEECHAM PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 21/11/2000	Date of completion of this report 20.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Fritz, M Telephone No. +49 89 2399 2792 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01522

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-11 as originally filed

Claims, No.:

1-14 as originally filed

Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/01522

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 14.

because:

☒ the said international application, or the said claims Nos. with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**~~V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;~~
citations and explanations supporting such statement**

1. Statement

Novelty (N)

Yes: Claims 1-13

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/01522

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 14 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 94 05659 A (SMITHKLINE BEECHAM PLC) 17 March 1994 (1994-03-17)
cited in the application
- D2: HALEBLIAN J ET AL: 'Pharmaceutical application of polymorphism' JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 58, no. 8, 1 August 1969 (1969-08-01),
pages 911-929, XP002020518 ISSN: 0022-3549

The present application relates to a special crystalline form of the maleic acid salt of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (claims 1-8), a process for preparing this compound (claim 9), a pharmaceutical composition thereof (claim 10), the compound according to claim 1 for the use as a therapeutically active substance (claim 11) and for use in the treatment and/or prophylaxis of diabetes mellitus (claim 12), the usage thereof for the manufacture of a medicament (claim 13) as well as a method of treatment by administering the compound according to claim 1 (claim 14)

For the assessment of the present claim 14 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a com-

pound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Example 1 of D1 describes a crystalline form of the maleate salt of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione which was characterized by ¹H NMR spectroscopy. It is stated in the present application that the compound described herein represents a different crystalline form of this known compound. There are no ¹H NMR data given in the present application, the different preparation procedures in the prior art and the present application make it however plausible that the maleate salt described in the present case is indeed a different crystalline form.

In D1 (p. 1, lines 24-25) it is emphasized that the salts of the compounds I (of which 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione is a representative) are characterized by significant formulation and bulk handling advantages.

D2 generally relates to polymorphism of pharmaceutically useful substances.

Therefore the subject-matter of claims 1-13 according to the present case is deemed to be novel in the sense of Article 33(2) PCT.

The problem of the present application was to provide 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione in a form which is particularly suitable for bulk preparation and handling.

Closest prior art is D1.

D1 emphasizes the significant formulation and bulk handling advantages of pharmaceutically acceptable salts of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (which was demonstrated in ex. 1 and also ex. 2 of D1). Polymorphism of pharmaceutically useful substances is a phenomenon which is well known in the art.

To solve the problem underlying the present case a person skilled in the art simply had to vary the preparation procedure described in examples 1 and 2 of D1 in order to arrive at a different crystalline modification of this known compound.

As it is already known from D1 that salts of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione show formulation and bulk handling properties which are superior to those of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione itself and polymorphism of this kind of substances is also known in the art (vide supra), an inventive activity was not necessary to solve the problem underlying the present case.

As the applicant has not demonstrated an unexpected effect which serves to distinguish the crystalline form of the maleate salt of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]-benzyl]thiazolidine-2,4-dione according to the present case further from the crystalline compound described in ex. 1 of D1, an inventive step in the sense of Article 33(3) PCT cannot be acknowledged for the subject-matter of claims 1-13.

Re Item VIII

Certain observations on the international application

Obviously claim 13 refers to the compound according to claim 1. This should be indicated in order to fulfill the requirements set forth in Article 6 PCT.

The terms "substantially" (claims 2-5), "isolated" (claim 6), "pure" (claim 7) as well as "certain complications" (claims 12-13) are vague and unclear and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Claims 2-5 contain a reference to the drawings.

According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

The relative term "elevated" employed in claim 9 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

It should be indicated in claim 1 that the nuclear magnetic resonance of ^{13}C was measured.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01522

The terms "compound (I)" as well as "denatured ethanol" employed in claim 9 should be defined therein (Art. 6 PCT).



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C07D 417/00	A2	(11) International Publication Number: WO 00/64893 (43) International Publication Date: 2 November 2000 (02.11.00)
(21) International Application Number: PCT/GB00/01522 (22) International Filing Date: 19 April 2000 (19.04.00) (30) Priority Data: 9909471.6 ✓ 23 April 1999 (23.04.99) GB 9912195.6 ✓ 25 May 1999 (25.05.99) GB (71) Applicant (for all designated States except US): SMITHKLINE BEECHAM PLC [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): BLACKLER, Paul, David, James [GB/GB]; SmithKline Beecham Pharmaceuticals, Old Powder Mills, Near Leigh, Tonbridge, Kent TN11 9AN (GB). GILES, Robert, Gordon [GB/GB]; SmithKline Beecham Pharmaceuticals, Old Powder Mills, Near Leigh, Tonbridge, Kent TN11 9AN (GB). MOORE, Stephen [GB/GB]; SmithKline Beecham Pharmaceuticals, Old Powder Mills, Near Leigh, Tonbridge, Kent TN11 9AN (GB). SASSE, Michael, John [GB/GB]; SmithKline Beecham Pharmaceuticals, Old Powder Mills, Near Leigh, Tonbridge, Kent TN11 9AN (GB).		(74) Agent: RUTTER, Keith; SmithKline Beecham, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB). (81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW). Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: NOVEL PHARMACEUTICAL (57) Abstract <p>A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "Polymorph") characterised in that it provides: (i) an infra red spectrum containing peaks at 1752, 1546, 1154, 621, and 602 cm⁻¹; and/or (ii) a Raman spectrum containing peaks at 1751, 1243 and 602 cm⁻¹; and/or (iii) a solid-state nuclear magnetic resonance spectrum containing peaks at 111.9, 114.8, 119.6, 129.2, 134.0, 138.0, 144.7, 153.2, 157.1, 170.7, 172.0 and 175.0 ppm; and/or (iv) an X-ray powder diffraction (XRPD) pattern which gives calculated lattice spacings of 6.46, 5.39, 4.83, 4.68, 3.71, 3.63, 3.58, and 3.48 Angstroms; a process for preparing such a compound, a pharmaceutical composition containing such a compound and the use of such a compound in medicine.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
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BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
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BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
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CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
2 November 2000 (02.11.2000)

PCT

(10) International Publication Number
WO 00/64893 A3

(51) International Patent Classification⁷: C07D 417/12,
A61K 31/427, A61P 3/10

Beecham Pharmaceuticals, Old Powder Mills, Near Leigh,
Tonbridge, Kent TN11 9AN (GB).

(21) International Application Number: PCT/GB00/01522

(74) Agent: RUTTER, Keith; SmithKline Beecham, Two New
Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(22) International Filing Date: 19 April 2000 (19.04.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9909471.6 23 April 1999 (23.04.1999) GB
9912195.6 25 May 1999 (25.05.1999) GB

(71) Applicant (for all designated States except US):
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Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BLACKLER, Paul,
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ning of each regular issue of the PCT Gazette.

(54) Title: THIAZOLIDINEDIONE DERIVATIVE AND ITS USE AS ANTIDIABETIC

(57) Abstract: A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "Polymorph") characterised in that it provides: (i) an infra red spectrum containing peaks at 1752, 1546, 1154, 621, and 602 cm⁻¹; and/or (ii) a Raman spectrum containing peaks at 1751, 1243 and 602 cm⁻¹; and/or (iii) a solid-state nuclear magnetic resonance spectrum containing peaks at 111.9, 114.8, 119.6, 129.2, 134.0, 138.0, 144.7, 153.2, 157.1, 170.7, 172.0 and 175.0 ppm; and/or (iv) an X-ray powder diffraction (XRPD) pattern which gives calculated lattice spacings of 6.46, 5.39, 4.83, 4.68, 3.71, 3.63, 3.58, and 3.48 Angstroms; a process for preparing such a compound, a pharmaceutical composition containing such a compound and the use of such a compound in medicine.

WO 00/64893 A3

INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/GB 00/01522

A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 05659 A (SMITHKLINE BEECHAM PLC) 17 March 1994 (1994-03-17) cited in the application the whole document, particularly page 2, lines 12-14	1,10
A	HALEBLIAN J ET AL: "Pharmaceutical application of polymorphism" JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 58, no. 8, 1 August 1969 (1969-08-01), pages 911-929, XP002020518 ISSN: 0022-3549 the whole document	1
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

Int'l Application No

PCT/GB 00/01522

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 99 31093 A (SMITHKLINE BEECHAM PLC) 24 June 1999 (1999-06-24) cited in the application the whole document	1,10
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 13, 14 (both partly)

Contrary to the requirements of Article 6 PCT, claims 13 and 14 do not clearly define the matter for which protection is sought. The search with regard to these claims has therefore been limited to the use of a polymorph as defined in claim 1.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

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